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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,313	11/28/2000	Elmar Reinhold Burchardt	LeA 32 701	8752

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,313	BURCHARDT ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *3-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/30/01 and 11/28/00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-5 are pending.

2. Since Applicant fails to state whether claim 5 is an immunoassay product or an immunoassay method, the Examiner considered claim 5 as a method claim. Accordingly, claim 5 is drawn to a non-elected invention.

3. Applicant's election with traverse of Group I, claims 1-3 and 5 (now 1-3), directed to a monoclonal antibody directed against an epitope within the 30 most N-terminal amino acids of human PIIINP, or an oligopeptide with the sequence derived from the N-terminal peptide is of Co12 domain of PIIINP, and the 30 most N-terminal amino acids of human PIIINP as the species filed on 4/6/07, is acknowledged.

Applicant's has not point out the supposed error in the restriction requirements. Accordingly the restriction requirement is proper.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 3 (non-elected species) and 4-5 (non-elected group) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

5. Claims 1-2 are under examination as they read on a monoclonal antibody directed against an epitope within the 30 most N-terminal amino acids of human PIIINP.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: the Post Office Address and Residence of inventor Elmar Reinhold Burchardt is altered without been initialed and dated. Any changes made in ink in the application or oath prior to signing should be initialed and dated by applicants prior to execution of the oath or declaration. The Office will not consider whether non-initialed and/or non-dated alterations were made before or after signing of the oath or declaration. See MPEP 605.04(a).

8. Applicant's IDS, filed 11/28/00 and 8/30/01, is acknowledged, however, references F1-F5 were crossed out because the English translation of the documents were not found. Applicant is invited to produce such documents.

9. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Page 6, line 24, page 7, line 12, page 29, Table 1, lines 10, 11, 16, 17, 23, 24, 30 and 31 and page 30, Table 2, lines 3-10 have described several amino acid and nucleic acid sequences that each must have a sequence identifier. Correction is required.

10. Claim 2 is objected to because of the following informalities:

A) the recitation "as described in 1." Should be changed to "according to claim 1,". Appropriate correction is required.

B) Claims 1-2 are missing an article such as "A" or "The" before the monoclonal antibody in the preamble of the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The recitation "characterized by preferential binding" in Claim 2 is indefinite because the narrow range binding within the broad range binding using the term "preferentially" renders the claim indefinite. The metes and bounds of such preferential binding are ambiguous and unclear and, in turn, the metes and bounds of the claimed "monoclonal antibody" are not defined.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which specifically bind to the 30 most N-terminal amino acids of human PIIINP consisting of amino acids 1-30 of SEQ ID NO: 2 for a diagnostic test, does not reasonably provide enablement for a monoclonal antibody directed against tan epitope within the 30 most N-terminal amino acids of human PIIINP in claim 1, wherein the antibody is characterized by preferential binding to trimeric PIIINP in claim 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The aminoterminal propeptide of type III procollagen (PIIINP) is cleaved off by a specific N-proteinase. The PIIINP molecule is an indicator of both the synthesis and the degradation of

type III collagen. PIIINP is a degradation product of type IIIpN collagen. PIIINP has a molecular weight of 42KD and contains three distinct domains: a triple-helical domain (col 3) in the middle of the colecule, the Col 1-domain at the aminoterminal and Col 2-domain at the carboxyterminal end of the propeptide. The measurement of PIIINP in human serum by radioimmunoassay facilitates the assessment of altered metabolism of type III collagen in situations such as fibrosis and malignancy. The monoclonal antibodies of the instant application used to measure trimeric PIIINP molecules and monomeric degradation products of PIIINP (see claims 1-2).

Since the claims are drawn to monoclonal antibodies are directed against an epitope within the 30 most N-terminal amino acids of human PIIINP, it is not clear whether the "30 most N-termina amino acids of human PIIINP" would include the signal peptide or without the signal peptide. Further, the skilled in the art would not expect a monoclonal antibody to the signal peptide would bind to the trimeric PIIINP. Furthermore, claiming the 30 most amino acids of biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is and of what compositions comprising that protein are made because different laboratories may have different numbering of the same protein. Recitation of amino acid position from the 30 most amino acid of a protein without providing SEQ ID NO for the protein does not provide a sufficient enabling description of the claimed invention. Accordingly, there is insufficient guidance and direction as to make and use the claimed monoclonal antibodies, wherein the antibodies directed against an epitope within the 30 most N-terminal amino acids of human PIIINP.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the 30 most amino acids of human PIIINP which the claimed antibodies raised against, the instantly recited 30 most amino acids of human PIIINP is unpredictable; thus the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Lotterer et al, 1993.

Lotterer et al teaches mouse monoclonal antibodies against human N-terminal peptide of type III procollagen (PIIINP) (see the title and abstract in particular).

While the prior art teachings may be silent as to the "30 most N-terminal amino acids of human PIIINP", "binding to trimeric PIIINP" or "subsequence from the col2 domain of PIIINP" per se; the product used in the reference method are the same as the claimed product. Therefore binding

to the 30 most amino acids of the PIIINP, trimeric PIIINP or subsequence from the col2 domain of PIIIP is considered inherent properties.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not bind to the 30 most N-terminal amino acids of human PIIINP, trimeric PIIINP or subsequence from the col2 domain of PIIINP recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

17. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Xie et al (1994).

Xie et al teach two monoclonal antibodies against N-terminal peptide of type III procollagen (PIIINP). Xie et al teach that the monoclonal antibodies recognize the conformational antigenic determinants. Further, the antibodies were also used for localization of type III procollagen in *human* heaptiocellular carcinoma tissues, cultured mouse fibroblasts and rat fibroblasts (see the abstract in particular).

While the prior art teachings may be silent as to the "30 most N-terminal amino acids of human PIIINP", "binding to trimeric PIIINP" or "subsequence from the col2 domain of PIIINP" per se; the product used in the reference method are the same as the claimed product. Therefore binding to the 30 most amino acids of the PIIINP, trimeric PIIINP or subsequence from the col2 domain of PIIIP is considered inherent properties.

Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not bind to the 30 most N-terminal amino acids of human PIIINP, trimeric PIIINP or the claimed oligopeptides recited in the claims. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

The reference teachings anticipate the claimed invention.

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

19. Claim 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brocks et al , 1993, (IDS ref.) in view of U.S. Pat. No. 5,512,283, as is evidenced by GenBank accession No. P02461.

Brocks et al study the uptake of the N-terminal propeptide of procollagen type III. Brocks et al use epitope scanning to determine the epitope recognized by the antiserum. 128 pins carrying peptides of 8 amino acids were synthesized. The first pin carried a peptide representing amino acids 19-26 of bovine N-terminal propeptide of procollagen type III (see page 383, under *Epitope scanning* in particular). That is (as is evidenced by GenBank accession no. P02461):

Bovine ^{19}TIILAQQE^{26}
Human ^{19}TIILAQQE^{26}

Bovine ^{20}IILAQQEA^{27}
Human ^{20}IILAQQEA^{27}

Bovine ^{21}ILAQQEAV^{28}
Human ^{21}ILAQQEAV^{28}

Bovine ^{22}LAQQEAVE^{29}
Human ^{22}LAQQEAVE^{29}

Bovine ^{23}AQQEAVEG^{30}
Human ^{23}AQQEAVEG^{30}

The bovine epitopes are identical to the human epitopes of the 30 most N-terminal amino acids of human PIIINP. Brocks et al further teach that all subsequent pins gave a positive signal (see page 384, 1st col., lines 3-4 in particular). That is the antiserum binds to the all epitopes (see Fig. 1 in particular).

The claimed invention differs from the reference teachings only by the recitation of a monoclonal antibody directed against an epitope within the 30 most N-terminal amino acids of human PIINP in claim 1.

Once the antigen of interest is selected, the use of that antigen in the known method of Kohler and Milstein will result in the expected hybrid cell lines and the specific monoclonal antibodies. Ex parte Erlich, 3 USPQ2d 1011, 1015 (BPAI 1986).

The `283 patent teaches that murine monoclonal antibodies to the antigen of interest are prepared by methods well known to those skilled in the art. BALB/c mice are immunized with specific

antigen preparations using a variety of protocols including use of immunological adjuvants such as complete and incomplete adjuvant. Spleen cells are prepared from mice shown to be producing antibodies of the proper specificity, and fused with cells from murine myeloma cell lines using established procedures (Kohler and Milstein, 1975, Nature 256:495-497) (see col., 14 lines 32-51 in particular).

Given that the antiserum binding to the epitopes above was week, it would have been obvious to one of ordinary skill in the art at the time the invention was made to to make a monoclonal antibody as taught by the `283 against the epitopes of the N-terminal propeptide of procollagen type III taught by the Brocke et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the monoclonal antibodies produced exhibit a high degree of specificity and great affinity.

The resultant antibody would bind to trimeric PIIINP, in absence of evidence to the contrary.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

20. No claim is allowed.

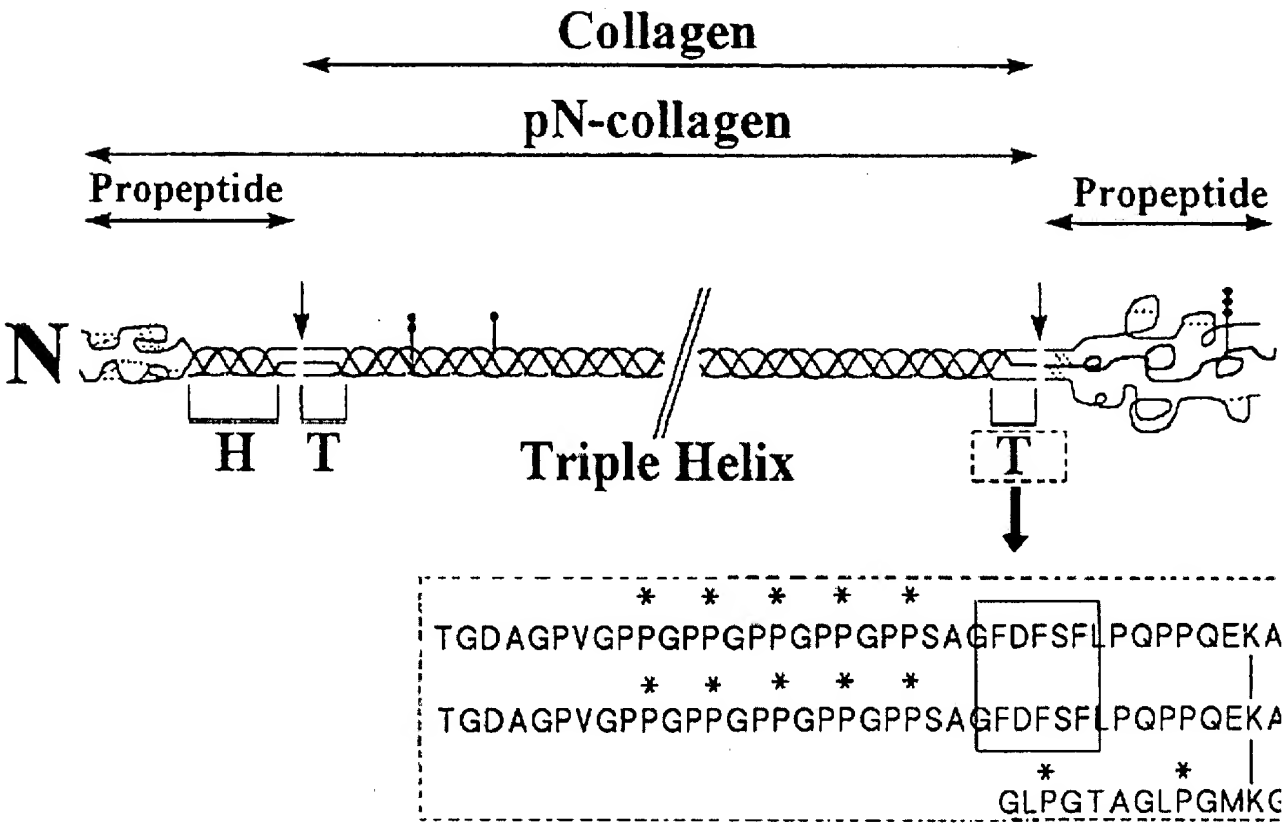
21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 15, 2007

Maher Haddad

Maher Haddad, Ph.D.
Primary Examiner
Technology Center 1600


Collagen
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